

# Prevalence of Sacroiliitis Assessed by Magnetic Resonance Imaging in a Pediatric Population with Inflammatory Bowel Disease

Duarte Alves<sup>1</sup>, Francisca Aguiar<sup>2</sup>, Ana Catarina Vieira<sup>3</sup>, Rita Fonseca<sup>4</sup>, Jorge Amil Dias<sup>5</sup>, Alberto Vieira<sup>6</sup>, Iva Brito<sup>2,7</sup>

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## Abstract

**Introduction:** The axial articular involvement in pediatric inflammatory bowel disease is frequent and often asymptomatic. There are no studies evaluating the sacroiliac joints assessed by magnetic resonance colonography or enterography performed in this population.

**Methods:** A cross-sectional study, including pediatric patients diagnosed with inflammatory bowel disease, previously submitted to magnetic resonance colonography or enterography, was performed. Two independent radiologists proceeded, independently and blindly, to magnetic resonance imaging analysis and identification of lesions suggestive of sacroiliitis. Parametric and non-parametric tests were used in statistical analysis to compare clinical and demographical variables in patients with or without sacroiliitis in magnetic resonance imaging.

**Results:** The study included 64 patients, 24 (37.5%) females, 54 (84.4%) with Crohn disease, 10 (15.6%) with ulcerative colitis, and an average age of  $15.1 \pm 2.8$  years. The prevalence of abnormalities suggestive of sacroiliitis in magnetic resonance was 31.2% ( $n = 20$ ). Females had a significantly higher prevalence of sacroiliitis (45.8% vs. 22.5% of positive magnetic resonance imaging in females and males, respectively,  $p = 0.048$ ) and those with positive magnetic resonance imaging had a shorter disease duration: 1.7 (0-10.5) vs. 3.2 (1-9.7) years,  $p = 0.001$ . Other factors, such as the type of inflammatory bowel disease, surgical history, current age, and age at diagnosis, were not associated with the presence of sacroiliitis.

**Discussion:** Our study showed that there is a high prevalence of asymptomatic sacroiliitis in children with inflammatory bowel disease (31.2%). Magnetic resonance colonography or enterography used to monitor the underlying disease, may contribute to the early identification of these patients.

**Keywords:** Adolescent; Child; Colitis, Ulcerative/complications; Crohn Disease/complications; Inflammatory Bowel Diseases; Magnetic Resonance Imaging; Portugal; Sacroiliitis/diagnostic imaging; Sacroiliitis/epidemiology

## Introduction

Inflammatory bowel disease (IBD) is a chronic and relapsing inflammatory condition that comprises Crohn disease and ulcerative colitis, and results from the interplay between genetic, immune, and environmental factors. Its precise etiology is not yet completely understood and, consequently, there is currently no causal treatment available.<sup>1</sup>

Inflammatory bowel disease has been increasingly recognized in the pediatric population, with estimates showing that 25% to 30% of Crohn disease patients and 20% of ulcerative colitis patients are under 20 years of age at diagnosis.<sup>2</sup> Currently, it is considered as one of the most frequent chronic diseases in the pediatric age.<sup>3</sup> Extraintestinal manifestations occur in 6% to 36% of IBD patients, which can be the initial presentation of the disease.<sup>4-8</sup>

In Crohn disease and ulcerative colitis, articular symptoms are the most common extraintestinal manifestation, with a reported prevalence of 16% to 33%.<sup>5,7-12</sup> These can be divided into peripheral and axial forms with a wide severity spectrum, ranging from transitory minor manifestations to persistent, destructive, and highly incapacitating ones.

Articular peripheral involvement in IBD includes arthralgia and peripheral arthritis, which can be associated with axial involvement, and that includes sacroiliitis.<sup>11,13</sup> This usually presents as inflammatory low back pain that can radiate to the buttocks, and is frequently associated with prolonged morning stiffness. However, in approx-

1. General Surgery Department, Dr. Nélio Mendonça Hospital, Funchal, Portugal

2. Rheumatology Department, São João Hospital Center, Oporto, Portugal

3. Radiology Department, Espírito Santo Hospital, Évora, Portugal

4. Rheumatology Department, Entre o Douro e Vouga Hospital Center, Santa Maria da Feira, Portugal

5. Pediatric Gastroenterology Department, São João Hospital Center, Oporto, Portugal

6. Radiology Department, São João Hospital Center, Oporto, Portugal

7. Faculty of Medicine, University of Porto, Porto, Portugal

### Corresponding Author

Francisca da Rocha Aguiar

francisca.ra@hotmail.com

Rua Dr. Joaquim Maia Aguiar, 81, 3º F, 4445-655 Ermesinde, Portugal

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imately 50% of cases, it can be asymptomatic thereby leading to difficulties and delay in the diagnosis.<sup>11,14</sup>

Sacroiliitis is the typical presenting lesion in axial involvement and is characterized by the presence of unilateral or bilateral inflammatory lesions (bone marrow edema) in sacroiliac joints. It is more frequent in Crohn disease and particularly in pediatric age group.

According to the 2009 Assessment of the Spondyloarthritis International Society (ASAS) classification criteria for axial spondyloarthritis,<sup>15</sup> a patient can be classified with the disease in the presence of sacroiliitis and one of the following manifestations/characteristics: inflammatory back pain, arthritis, enthesitis, uveitis, dactylitis, psoriasis, IBD, good response to non-steroidal anti-inflammatory drugs, family history of spondyloarthritis, positivity for antigen HLA-B27, or elevated C-reactive protein.

Sacroiliitis described by the ASAS group includes radiographic sacroiliitis defined by the modified New York criteria<sup>16</sup> or active (acute) inflammation suggestive of sacroiliitis on magnetic resonance imaging (MRI), the latter contributing to an earlier identification of these patients and improvement in the prognosis. The detection of sacroiliitis by conventional radiography and computed tomography (CT) presents several limitations, as they only allow the visualization of structural lesions while early inflammatory changes are not detected.<sup>17</sup>

Since the 1990s MRI has shown to be a very useful tool in the assessment of the early inflammation of sacroiliac joints and vertebral spine. According to ASAS/outcome measures in rheumatology (OMERACT) criteria, a positive MRI is defined by the presence of one active lesion (bone marrow edema) in at least two consecutive cuts or two or more lesions in one cut.<sup>15</sup>

Enterography by CT or MRI is a valuable tool in the evaluation of IBD, namely for studying the intestinal activity of the disease. However, the European Crohn and Colitis Organization (ECCO) recommends the preferential use of MRI, due to the risk of higher radiation exposure with CT, which increases with the repeated evaluations that are frequently needed.<sup>18</sup>

So far, there have been no studies investigating the presence of asymptomatic sacroiliitis in MRI enterography/colonography performed in this population. Therefore, this work aims to investigate the prevalence of asymptomatic sacroiliitis in a population of patients with juvenile IBD diagnosis.

The secondary aim was to identify the demographic and clinical variables associated with the presence of sacroiliitis.

## Methods

This cross-sectional study included pediatric patients (aged 18 years old or less) diagnosed with juvenile IBD (Crohn disease and ulcerative colitis) and attending pediatric gastroenterology clinic in a tertiary university hospital, and previously submitted MRI colonography or enterography. These exams were performed in the context of IBD disease activity evaluation and, therefore, the presence of inflammatory lesions in sacroiliac joints was not investigated.

The following exclusion criteria were defined: patients with incomplete clinical data or lost to follow-up and/or the inability to visualize sacroiliac joints in MRI enterography/colonography.

Data from the patients was obtained by consulting the hospital medical records.

Besides MRI enterography/colonography findings, demographic (birth date, gender) and clinical (diagnosis, diagnosis date, disease duration, surgeries, articular complaints, previous diagnosis of spondyloarthritis, or other juvenile rheumatic disease) information was also collected.

### Sacroiliac joint assessment by MRI

MRI enterography was performed using a field of view (FOV) limited by the 11<sup>th</sup> dorsal vertebra and femoral head, allowing for the assessment of sacroiliac joints.

T1 and T2-weighted multiplanar sequences were obtained, with and without fat saturation (FS), and dynamic study after paramagnetic contrast agent (gadolinium) administration was performed.

(i) Coronal and axial LAVA: three minutes after contrast agent administration, an acquisition time of 20 s, FOV 480 x 480 mm, matrix 384 x 224, slice thickness 3 mm, gap 1.5 mm, spatial resolution 1.1 x 2.1 x 3 = 6.9  $\mu$ L, 1 excitation (NEX 1), echo time (ET) 1.88 m/s, repetition time (RT) 3.95 m/s, and flip angle 15°.

(ii) Axial T1 FS: four minutes after contrast agent administration, acquisition time of 60 s, FOV 440 x 440 mm, matrix 512 x 224, slice thickness of 7 mm, gap 7 mm, spatial resolution of 0.9 x 1.9 x 7 = 11,97  $\mu$ L, NEX 1, ET 1.52 m/s, RT 205 m/s, and flip angle 8°.

Two independent radiologists proceeded, independently and blindly, to the MRI analysis and identification of lesions suggestive of sacroiliitis.

The changes identified were classified as positive (inflammatory) according to ASAS classification: presence of subchondral or periarticular marrow edema of the sacroiliac joint in one slice for bilateral alterations or in two consecutive slices for unilateral ones.

Sacroiliac joints were categorized as normal, positive (unilateral/bilateral), and doubtful.

The assessments of both observers were compared in order to have a final classification. In case of discordance, the definitive category was defined by consensus.

**Statistical analysis**

Statistical analysis was performed using SPSS 23.0 software. In order to study possible factors associated with the presence of sacroiliitis in MRI, clinical and demographic variables were compared between the group with and without sacroiliitis.

Qui-square test was used to compare categorical variables and *Student’s t*-test and non-parametric tests (Mann-Whitney U test) to compare the continuous variables between both groups. Statistical significance ( $\alpha$ ) was defined as 0.05.

**Results**

Demographic and clinical data from the patients included in the study are presented in Table 1.

Sixty-four patients were included, 24 (37.5%) females, 54 (84.4%) with Crohn disease, 10 (15.6%) with ulcerative colitis, and an average age of  $15.1 \pm 2.8$  years.

The mean age at IBD diagnosis was  $12.1 \pm 3.3$  years and the median disease duration was 2.77 (0-10.5) years.

The disease severity was evaluated based on the abdominal surgery history. The majority of the patients had not been submitted to any surgery (n = 51, 79.7%), 12 (18.8%) were submitted to one, and one patient (1.6%) underwent more than one.

Clinical information regarding extraintestinal osteoarticular manifestations and HLA-B27 antigen were not available. Among the 64 patients, 17 (26.6%) presented nonspecific arthralgia and, of these, 5 (7.8%) had axial complaints.

The prevalence of abnormalities suggestive of sacroiliitis in MRI was 31.2% (n = 20) (Table 2). In 15 (23.4%) of those patients, the findings were bilateral and unilateral in the other five (7.8%).

Regarding the comparison of clinical characteristics between patients with and without a “positive” MRI (Table 3), the prevalence of sacroiliitis was similar among those with Crohn disease and ulcerative colitis. There were also no differences between patients with or without prior surgery history.

In what concerns gender, the prevalence of sacroiliitis was significantly more frequent in females (45.8%) compared to males (22.5%),  $p = 0.004$ .

There were no statistically significant differences in respect to age of diagnosis or current age. Nevertheless, as to disease duration, those with positive MRI had a shorter disease duration: 1.7 (0-10.5) vs. 3.2 (1-9.7) years,  $p = 0.001$ .

The prevalence of sacroiliitis was higher in patients with nonspecific articular complaints (45% vs. 23.4%,  $p = 0.028$ ), despite no previous diagnosis of spondyloarthritis.

**Discussion**

Extraintestinal manifestations, namely spondyloarthritis, have an estimated prevalence of 9%-46% in patients with IBD diagnosis.<sup>4-8</sup>

In the pediatric age, although this estimate is less accurate, it seems to range from 9% to 24%.<sup>9</sup>

Inflammatory lesions affecting sacroiliac joints can develop early and usually follow an independent course from the underlying disease. In addition, they are often asymptomatic for years and that leads to a late diagnosis when there is already irreversible structural damage.<sup>14</sup>

MRI enterography or colonography are frequently performed in patients with IBD. These exams, despite not being protocolled for the diagnosis of sacroiliitis, could be useful in the early detection of inflammatory lesions, contributing to a timelier diagnosis, mainly in the sub-clinical phase, as shown in this study. However, performing specific protocolled imaging tests that evaluate these joints should always be considered to establish a definitive diagnosis.<sup>19</sup>

This was the first work to study sacroiliac joints by MRI enterography or colonography in pediatric IBD patients.

**Table 1. Demographic and clinical characteristics of patients included in the study**

Characteristics	n (%)
	Mean $\pm$ SD Median (min.-max.)
IBD	
Crohn disease	54 (84.4)
Ulcerative colitis	10 (15.6)
Gender	
Female	24 (37.5)
Male	40 (62.5)
Age (years)	15.1 $\pm$ 2.8
Age at diagnosis (years)	12.1 $\pm$ 3.3
Disease duration (years)	2.77 (0-10.5)
Surgery	
Yes	13 (20.3)
No	51 (79.7)
Articular complaints	
Yes	17 (26.6)
No	47 (73.4)

IBD - inflammatory bowel disease; max. - maximum; min. - minimum; SD - standard deviation.

**Table 2. Sacroiliitis prevalence in the population studied**

Characteristics	n	%
MRI negative	44	68.75
MRI positive	20	31.2
Unilateral	5	7.8
Bilateral	15	23.4

MRI - magnetic resonance imaging.

independence of sacroiliac joint involvement from the underlying disease course.

In this study, sacroiliitis was more frequent in female patients, which is opposite to what has been previously described about its distribution according to gender, as rheumatic manifestations associated with IBD present a male:female ratio of 3:1.<sup>1</sup> These findings can only be confirmed in a study with a larger sample size.

**Table 3. Comparison of the clinical characteristics between patients with and without sacroiliitis in magnetic resonance enterography or colonography**

Characteristics	"Normal" MRI n = 44 (68.8%)	"Positive" MRI n = 20 (31.3%)	p
	n (%) Mean ± SD Median (min.-max.)	n (%) Mean ± SD Median (min.-max.)	
IBD			NS
Crohn disease	37 (68.5)	17 (31.5)	
Ulcerative colitis	7 (70)	3 (30)	
Gender			0.04*
Female	13 (54.2)	11 (45.8)	
Male	31 (77.5)	9 (22.5)	
Age (years)	15.1 ± 3.2	15.3 ± 1.6	NS
Age at diagnosis (years)	11.6 ± 3.6	13.0 ± 2.29	NS
Disease duration (years)	3.2 (1-9.7)	1.65 (0-10.5)	0.001†
Surgery			
Yes	11 (25)	18 (90)	NS
Articular complaints			0.028*
Yes	8 (18.2)	9 (45)	
No	36 (76.6)	11 (23.4)	

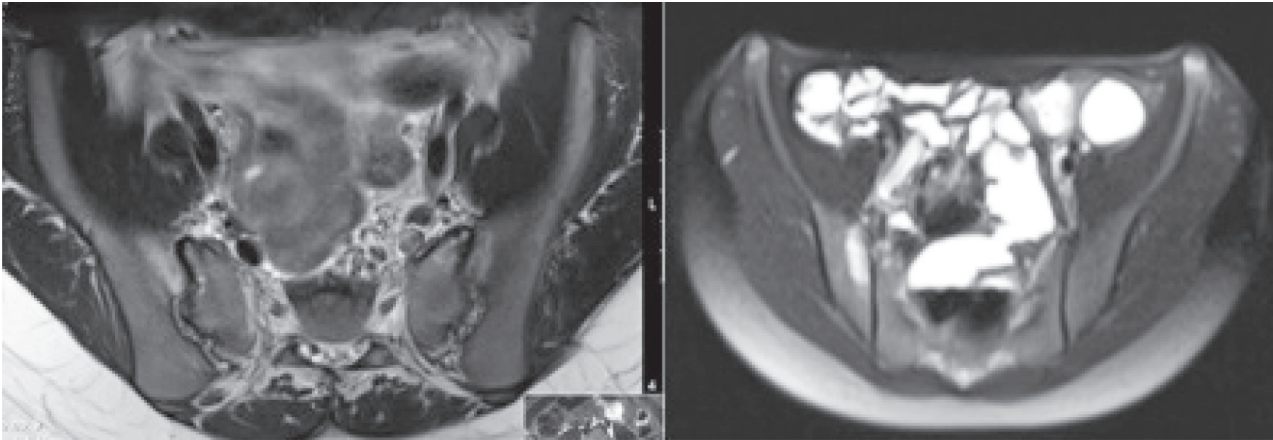
IBD - inflammatory bowel disease; max. - maximum; min. - minimum; MRI - magnetic resonance imaging; NS - not significant; SD - standard deviation. \* Fisher's exact test. † Mann-Whitney U test.

Among the 64 patients evaluated, 20 (31.2%) presented abnormalities suggestive of sacroiliitis. This prevalence is slightly higher than that previously reported in the scientific literature. A possible explanation for this result might be the scarcity of data concerning the prevalence of these lesions in asymptomatic patients, which is thought to be underestimated.

Regarding the possible factors associated with the presence of sacroiliitis in MRI enterography or colonography, we could not find significant differences between the patients with Crohn disease and ulcerative colitis, although a higher prevalence of these manifestations in Crohn disease is well documented in previous studies. It must be noted that MRI tests were performed less frequently in ulcerative colitis patients, leading to a reduced sample of these patients compared to Crohn disease. There were also no differences between patients with or without previous surgical history (used as an indirect measure of IBD activity), confirming the

As expected, considering the previously exposed considerations, there were no significant differences in current age or age at IBD diagnosis. Nevertheless, patients with sacroiliitis had lower IBD duration. IBD-related sacroiliitis does not correlate with underlying disease activity and, in most cases, follows an independent course, which agrees with the presented data. Furthermore, it is believed that asymptomatic lesions prevalence can reach 50%.<sup>14</sup> Our study reinforces the fact that these lesions occur early in the course of IBD and, in most cases, are asymptomatic.

Finally, patients with arthralgia were also the ones who presented sacroiliitis in MRI more frequently. However, specific details about the rhythm and localization of these symptoms were not described in the clinical records, which represents a major limitation in the analysis and appreciation of this result. Inflammatory back pain is included in the ASAS criteria for spondyloarthritis, but these patients often present peripheral



**Figure 1.** Contrast-enhanced T2-weighted magnetic resonance enterography image showing high signal on the sacral and iliac sides of right sacroiliac joint, compatible with a “positive” MRI.

arthralgia as the initial musculoskeletal manifestation, whereby they should be evaluated by a rheumatologist, aiming at an early diagnosis.

The main limitations of this study include its design (cross-sectional) and the small sample size, which hinder the interpretation of these results and the generalizability of our conclusions. In addition, all of the information was analyzed retrospectively, and it was not possible to obtain data about some clinical characteristics, namely osteoarticular manifestations and antigen HLA-B27 positivity, which would allow the classification as axial spondyloarthritis according to ASAS criteria (even in the absence of radiographic data).

Given the high prevalence of sacroiliitis in patients with pediatric IBD, it is of the utmost importance to raise awareness among pediatric gastroenterologists so that there is high clinical suspicion leading to an early referral to pediatric rheumatology clinic.

Moreover, greater attention should be paid by the radiologists analyzing MRI enterography and colonography in order to detect sacroiliac joints lesions, which could make a difference, as these are often the only identifiable abnormalities in asymptomatic patients.

#### WHAT THIS STUDY ADDS

- There is a high prevalence of asymptomatic sacroiliitis in children with inflammatory bowel disease (31.2%).
- Sacroiliitis was more frequently detected in female patients and those with a shorter duration of the disease.
- Magnetic resonance colonography or enterography performed to monitor the underlying disease, may contribute to the early identification of these patients, as these exams can show inflammatory lesions (bone marrow edema) in the sacroiliac joints.

#### Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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#### Consent for publication

Consent for publication was obtained.

#### Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

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### Prevalência de Sacroileíte Imagiológica numa População Pediátrica com Doença Inflamatória Intestinal

#### Resumo:

**Introdução:** O envolvimento articular axial na doença inflamatória intestinal (DII) pediátrica é frequente e comumente assintomático. Não existem estudos que avaliem a presença de sacroileíte assintomática por enterografia/colonografia por ressonância magnética (RM) nesta população.

**Métodos:** Estudo transversal incluindo doentes em idade pediátrica com diagnóstico de DII que tinham sido submetidos previamente a colonografia ou enterografia por RM. Dois radiologistas independentes procederam à leitura das RM e identificação de lesões de sacroileíte, de forma independente e cega. Testes paramétricos e não paramétricos foram usados na análise estatística para comparação de variáveis clínicas e demográficas entre doentes com e sem sacroileíte na RM.

**Resultados:** Foram incluídos 64 doentes, 24 (37,5%) do sexo feminino, 54 (84,4%) com doença de Crohn e 10 (15,6%) com colite ulcerosa, com uma média de idade de 15,1 ± 2,8 anos.

Verificou-se que em 20 (31,2%) existiam alterações sugestivas de sacroileíte na RM. Verificou-se que a presença de sacroileíte foi significativamente mais frequente no sexo feminino (45,8% *versus* 22,5%,  $p=0,04$ ) e nos doentes com menor duração da doença (1,65 [0-10,5] *versus* 3,2 [0-1,8],  $p=0,01$ ). Não se verificaram diferenças com significado estatístico no que diz respeito à idade ao diagnóstico, idade atual, tipo de DII ou historial cirúrgico.

**Discussão:** Este estudo comprovou a existência de uma elevada prevalência de sacroileíte em doentes com DII em idade pediátrica. A colonografia ou enterografia por RM, realizadas no âmbito da monitorização da doença de base, podem contribuir para a identificação precoce destes doentes.

**Palavras-Chave:** Adolescente; Colite Ulcerativa/complicações; Criança; Doença de Crohn/complicações; Doenças Inflamatórias Intestinais; Ressonância Magnética; Portugal; Sacroileíte/diagnóstico por imagem; Sacroileíte/epidemiologia